REMARKS

This will acknowledge the Examiner's requirement of restriction in the Office Action mailed January 22, 2002, and Applicants' subsequent election, with traverse, of the invention of Group I, Claims 1-20, 29 and 33. In the outstanding Office Action mailed June 6, 2002, the Examiner has made the requirement of restriction final, having earlier found Applicants' traverse of the restriction requirement not persuasive, and has withdrawn from consideration Claims 21-28, 30-32, and 34-38 as being drawn to non-elected inventions.

Responsive to the Examiner's action, Applicants have herein cancelled all of the claims directed to non-elected inventions, *i.e.*, Claims 21-28, 30-32, and 34-38.

Claims 1-20, 29 and 33 stand rejected under 35 U.S.C. § 103(a) as obvious over the disclosure of Chahwala *et al.* U. S. Patent No. 6,080,761 ("the '761 patent") taken in view of Foster *et al.* U. S. Patent No. 6,333,342 B1 ("the '342 patent"). The Examiner contends that the '7616 patent teaches the R(+) isomer of amlodipine to be "a well-known channel-blocking agent having vasodilatory activity, and that the '342 patent teaches the S(–) isomer of amlodipine to be "well-known for its anti-hypertensive activity."

Based on the above-described disclosures that the Examiner contends are made by the cited references, the Examiner has taken the position that "one skilled in the art would assume that combining of the two isomers into a single composition possessing the same anti-hypertensive activity will give an additive effect in the absence of evidence to the contrary."

The Examiner's conclusions are traversed by Applicants on the grounds that both of the cited references teach away from a combination of their teachings as proposed by the Examiner. The '761 patent teaches use of only the R(+) isomer of amlodipine as a potent inhibitor of smooth muscle cell migration that provides treatment of, *e.g.*, re-stenosis, atherosclerosis, and endometriosis. The '761 patent further teaches that "the R(+) isomer has little or no calcium channel blocking activity" and, accordingly, that "[t]he R(+) isomer thus provides a means of treating conditions involving smooth muscle cell migration without any concomitant cardiovascular effects." [Emphasis added]

The '342 patent teaches use of only the S(–) isomer of amlodipine, *i.e.*, "substantially free of the R(+) stereoisomer", as an effective antihypertensive agent for both systolic and diastolic hypertension, and angina, while "reducing or avoiding undesirable adverse effects, such as headache and edema, dizziness, flushing, palpitation, fatigue, nausea, abdominal pain and somnolence which are associated with the administration of the racemic mixture of amlodipine."

At Column 10, line 53 to Column 11, line 4 of the '342 patent the expression "substantially free of its R(+) stereoisomer" is defined as meaning that "the composition contains a greater proportion or percentage of the S(–) isomer of amlodipine in relation to the R(+) isomer of amlodipine,

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